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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,891	05/18/2006	Dominique Jean-Pierre Mabire	PRD2120USPCT1	8597
27777 7590 09/28/2009 PHILIP S. JOHNSON JOHNSON & JOHNSON ONE JOHNSON & JOHNSON PLAZA NEW BRUNSWICK, NJ 08933-7003				
EXAMINER MCDOWELL, BRIANE				
ART UNIT		PAPER NUMBER		
1624				
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09/28/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/595,891

**Applicant(s)**

MABIRE ET AL.

**Examiner**

BRIAN MCDOWELL

**Art Unit**

1624

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 17-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

/BEM/

**DETAILED ACTION**

***Status of Claims***

Claims 17-21 are pending in the instant application.

***Status of Restriction Requirement***

Applicant is reminded that the elected invention is drawn to compounds of the general formula (I) stated in claim 1, wherein X is N or CR<sup>7</sup>, **wherein R<sup>7</sup> = H**.

Claim 1 should be amended accordingly to embrace the elected invention.

***Status of Claim Objections***

Applicant's amendment of claim 19, see Remarks, filed 7/23/2009, with respect to the Non-Final Office Action mailed 4/29/2009, has been fully considered and the objection has been overcome. However, claim 20 is still objected to. The claim should be written as "A compound selected from" or similar language; followed by the claimed chemical structures. The text within claim 20 describing the compound number (e.g., compounds No 16, etc.) is not required. Additionally, said text (e.g., compound 16, 144, and 145) should be removed from under the claimed structures to clearly depict the subject matter being claimed. Appropriate correction is required.

***Status of Rejections***

***Double Patenting***

**The ODP rejections of claims 17-21 are maintained over copending applications 10/596086 and 10/595882 for the reasons of record.**

***35 USC § 112 (1<sup>st</sup> Paragraph)***

Applicant's cancellation of claim 22, see Remarks, filed 7/23/2009, with respect to the Non-Final Office Action mailed 4/29/2009, has been fully considered and the rejection has been overcome.

***New Objections and Rejections***

***Claim Objections***

Claim 17 is objected to for the following informality:

"PiperidinylC<sub>1-6</sub>alkylaminocarbonyl" is recited twice as a substituent for moieties R<sup>8,10,11</sup> (see page 3, lines 3-4). Additionally, "arylC<sub>1-6</sub>alkyl" is recited twice as a substituent for moiety R<sup>12</sup> (see page 4, lines 3 and 6). Please delete accordingly and throughout where appropriate.

***Claim Rejections - 35 USC § 112 (1<sup>st</sup> Paragraph)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-19 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "pharmaceutically acceptable salts" and "stereo-chemically isomeric forms thereof" of the instantly claimed compounds, does not reasonably provide enablement for N-oxides and all addition salts of said compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Pursuant to *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444. Analysis is described below:

(A) Breadth of claims: The formula I is drawn to every possible N-oxide and addition salt of the compound of formula I. The claims cover compounds of the formula I, their respective N-oxides, and addition salts that may afford thousands of structurally different entities; thus the claims are very broad.

(B) The nature of the invention: 2-quinoxalinones and 2-quinolinones as poly(ADP-ribose)polymerase-1 inhibitors.

(C) State of the Prior Art: Chemistry is unpredictable. See *In Re Marzocchi and Horton* 169 USPQ at 367 paragraph 3:

*"Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research*

*articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task.*

*In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious)" Dorwald F. A. Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.*

In addition to the above statement, "addition salts" may encompass salts of the instantly compounds that may not be suitable for administration to a patient. "Addition salts" may include heavy metal and toxic salts of the instant compounds that are expected to be inoperable in a pharmaceutical setting.

(D) Skill of those in the art: The level of skill in the art is high.

(E) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(F) Direction or Guidance: Little guidance or direction is provided by applicant in reference to making N-oxides and every addition salt of compounds of the formula I. Specification offers no teachings or suggestion as to how to make and use these compounds. Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when



the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.”;

(G) Working Examples: The compound core depicted with specific substituents represent a narrow subgenus for which applicant has provided sufficient guidance to make and use; however, this disclosure is not sufficient to allow extrapolation of the limited examples to enable the scope of the compounds instantly claimed. Applicant has provided no working examples of any compounds where the compound of formula I did not contain the variables previously mentioned above in the present application.

Within the specification, “specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula.” See MPEP 608.01(p).

(H) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome. Applicant fails to provide guidance and supporting information for how to make and/or use the thousands of other compounds which are encompassed by the claims, therefore undue experimentation would be expected.

Due to the level of unpredictability in the art, the very limited guidance provided, and the lack of working examples, the applicant has shown lack of enablement. MPEP

2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

### ***Conclusion***

No claims are allowed.

#### **Potential Reasons for Allowance**

Claims 17-21 may be allowable if the appropriate terminal disclaimers are filed and the objections/rejections stated above are addressed. The instantly claimed compounds are free of the prior art with respect to moieties representing the substituent R<sup>3</sup> on the compound's core, where in said prior art said substituent is not taught or fairly suggested.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRIAN MCDOWELL whose telephone number is (571)270-5755. The examiner can normally be reached on Monday-Thursday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/B.E.M./  
Patent Examiner, Art Unit 1624

**/James O. Wilson/  
Supervisory Patent Examiner, AU 1624**